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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,191	08/24/2001	Hugh Redmond Brady	1377-0170P	9468
2292	7590	08/23/2004	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			SULLIVAN, DANIEL M	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 08/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/914,191

Applicant(s)

BRADY ET AL.

Examiner

Daniel M Sullivan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 17 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-11 is/are pending in the application.
- 4a) Of the above claim(s) 8-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 7 and 11 is/are rejected.
- 7) ☒ Claim(s) 6 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This Non-Final Office Action is a reply to the Paper filed 17 May 2004 in response to the Non-Final Office Action mailed 10 September 2003. Claims 8-10 were withdrawn from consideration and claims 1-7 and 11 were considered in the 10 September Office Action. Claim 5 was cancelled and claims 1, 7 and 11 were amended in the 17 May Paper. Claims 1-4 and 6-11 are pending and claims 1-4, 6, 7 and 11 are under consideration.

#### ***Response to Amendment***

##### Specification

Objection to the specification because the description of Figure 13 does not match the drawing is withdrawn in view of the amendment to the specification.

##### Claim Objections

Objection to claims 7 and 11 as directed to nonelected subject matter (*i.e.*, SEQ ID NO: 2-6) is withdrawn.

##### Claim Rejections - 35 USC § 101

Rejection of claim 11 under 35 U.S.C. 101 as directed to non-statutory subject matter is withdrawn.

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Claim Rejections - 35 USC § 101/112, first paragraph

The Declaration under 37 CFR 1.132 and Exhibit A filed 17 May 2004 is sufficient to overcome the rejection of claim 11 based upon 35 USC § 101 and 112, first paragraph, as lacking a substantial utility.

The declaration identifies the protein encoded by SEQ ID NO: 1 as IHG-1, which is disclosed in Table 1 of the originally filed specification as being induced in mesangial cells cultured in high glucose. Further, Exhibit A confirms that SEQ ID NO: 1 is upregulated in renal biopsies from patients with diabetic nephropathy. Thus, the preponderance of the evidence indicates that the claimed nucleic acid would be useful at least as a diagnostic marker for diabetic nephropathy as asserted in the specification.

Claim Rejections - 35 USC § 112

Rejection of claims 1-7 and 11 under 35 U.S.C. 112, second paragraph, as being indefinite for the reasons set forth in the 10 September Office Action is withdrawn.

Claim Rejections - 35 USC § 102

Claims 1-3 stand rejected under 35 U.S.C. 102(b) as being anticipated by Murphy *et al.* (1998) *J. Am. Soc. Nephrol.* 9:637A as evidenced by Riser *et al.* (1998) *J. Am. Soc. Nephrol.* 9:827-836.

Although the limitation of the method to culturing the mesangial cells in the presence of TGF- $\beta$ 1 was previously indicated to be free of the art, upon further consideration it is clear that the limitation is inherent to the method of Murphy *et al.* Riser *et al.* teaches that mesangial cells

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cultured in the presence of elevated glucose secrete TGF- $\beta$ 1 (see especially Figure 1 and the caption thereto). In the method of Murphy *et al.*, mesangial cells are cultured in 30 mM glucose for 7 days, which riser teaches would lead to secretion of TGF- $\beta$ 1. Therefore, for reasons of record and herein above, the method of Murphy *et al.* includes culturing the cells in the presence of TGF- $\beta$ 1 and anticipates the instant claims 1-3.

### ***New Grounds***

#### Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amended claim is now directed to an isolated “gene” encoded by a sequence of SEQ ID NO: 1. The term “gene” is commonly understood in the art to encompass at least transcriptional regulatory elements in addition to coding sequence. In contrast, SEQ ID NO: 1 appears to be a cDNA and therefore lacks transcriptional regulatory elements. Thus, it is unclear whether applicant is claiming a gene comprising SEQ ID NO: 1 or is claiming a nucleic acid encoded by SEQ ID NO: 1.

#### Claim Rejections - 35 USC § 102

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 7 are rejected under 35 U.S.C. 102(b) as anticipated by Murphy *et al.* (1998) *J. Am. Soc. Nephrol.* 9:637A as evidenced by Riser *et al.* (1998) *J. Am. Soc. Nephrol.* 9:827-836.

Murphy *et al.* as evidenced by Riser *et al.* teaches a method according to the limitations of claim 1 (*Id.*). Although Murphy *et al.* does not disclose that the gene differentially expressed in the method is a gene of SEQ ID NO: 1, the method steps disclosed by Murphy *et al.* and the mesangial cells used in the method are the same as those set forth in the instant claims and would logically lead to induction of the gene comprising SEQ ID NO: 1 as recited in claim 7. Thus, the limitations of claim 7 are anticipated by the teachings of Murphy *et al.* as evidenced by Riser *et al.*

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy *et al.* as applied to claim 1 above, and further in view of Riser *et al.* (*supra*).

Murphy *et al.* teaches a method for identifying a gene which may be involved with the presentation of diabetic nephropathy comprising culturing cells in a medium comprising glucose at a concentration sufficient to induce differential expression of a gene susceptible to differential expression, which medium Riser *et al.* teaches would also comprise TGF- $\beta$ 1 (*Id.*). Murphy *et al.* further teaches identifying the gene so induced by suppression subtractive hybridization.

Murphy *et al.* does not teach the method wherein the mesangial cells are subjected to mechanical strain according to claim 4.

Riser *et al.* teaches an *in vitro* mesangial cell model of diabetic nephropathy and that high glucose and mechanical strain act in an additive manner to increase TGF- $\beta$ 1 secretion, which results in increased accumulation of collagen relative to the accumulation of collagen in the presence of high glucose alone (see especially Figure 1 and Figure 5 and the captions thereto).

Riser *et al.* further teaches that the mechanical strain modeled in their *in vitro* system is consistent with what is estimated to result from oscillations in intraglomerular pressure (second full paragraph in the right column on page 834) and that recent findings “suggest that the net

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accumulation of [extracellular matrix] may only occur when both hyperglycemia and glomerular hypertension are present” (first full paragraph on page 828).

It would have been obvious to one of ordinary skill in the art at the time the invention was filed to modify the method of Murphy *et al.* to include the combination of mechanical strain with high glucose as taught by Riser *et al.* Riser *et al.*, teaches that elevated glucose and mechanical strain have an additive effect on the relevant pathological parameter of increased accumulation of extracellular matrix, and that it is likely that hyperglycemia and mechanical strain are both present in the diabetic kidney. Thus, at the time of filing it was known that mechanical strain could be modeled in *in vitro* cultures of mesangial cells, and the skilled artisan would be motivated to combine mechanical strain with hyperglycemia in the method of Murphy *et al.* in order to more closely model the pathophysiological state of diabetic nephropathy as suggested by Riser *et al.*

Absent evidence to the contrary, the skilled artisan would have a reasonable expectation of success in combining these teachings because the addition of mechanical strain would not be expected to interfere with the analytical method of Murphy *et al.* in any way.

For these reasons, the method of claims 1 and 4, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing.

#### ***Allowable Subject Matter***

Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.



***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M Sullivan, Ph.D.  
Examiner  
Art Unit 1636

  
PRIMARY EXAMINER